Section II (Remarks)

Rejections under 35 U.S.C. 112, Second Paragraph

Claims 1-17 were rejected under 35 U.S.C. 112, second paragraph, as indefinite. The basis for the rejection was that the phrase "the ratio of both polymers" was purportedly unclear. In response, Claims 1 and 11 have been amended to specify that the weight ratio of "both polymers" refers to the ratio of the biodiegradable polymer to the polyoxyethylene-derived polymer. Support for the amendment is found in the specification, at least, on page 8, lines 12-13.

The amendment to Claims 1 and 11 obviates the rejection, and, accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. 102 (b)

Claims 1-17 were rejected under 35 U.S.C. 102 (b) as anticipated by U.S. Patent No. 5,962,566 to Grandfils et al. ("Grandfils"). The rejection is respectfully traversed if applied to the amended claims.

Claims

Claim 1 is directed to a method of preparing nanoparticles having a size of less than 1 μm, for the administration of active ingredients. As currently amended, the method involves the steps of: a) dissolving a biodegradable polymer together with a polyoxyethylene-derived block copolymer in a nonpolar organic solvent, then adding, with stirring, the solution obtained to a polar phase, wherein the biodegradable polymer has low solubility, precipitating the polymer and forming the nanoparticles. The organic solvent is eliminated, and the particles are isolated. The weight ratio of the biodiegradable polymer to the polyoxyethylene-derived polymer is between 1:0.1 and 1:3.

The active ingredient is dissolved in the organic solvent before or after the biodegradable polymer is dissolved in the nonpolar organic solvent, or is dissolved in a small volume of the aqueous phase, which is then dispersed in the organic solvent.

Grandfils

Grandfils does not disclose or suggest using a non-polar solvent to dissolve a biodegradable polymer and a polyoxyethylene-derived block copolymer just prior to their mixture with the aqueous phase.

Grandfils may use a non-polar organic solvent (methylene chloride), but only to prepare an intermediate blend of polymers. The organic solvent is removed, then a water soluble organic solvent, such as DMSO, acetone, RHF, 1,3-dioxolane, DMF, or mixtures thereof, is used (see col. 3, lines 64-67 and Claim 5).

Analysis

The use of a polar solvent, as taught by Grandfils, is completely different, in this context, from the use of a non-polar solvent as instantly claimed. If it was the same, the Grandfils would not have gone through the effort of evaporating a non-polar solvent only to add a second, polar solvent.

Further, Grandfils requires a solvent evaporation step, because he requires that the polymers be dissolved in a polar organic solvent. This is in stark contrast to the claimed method, which requires that the polymer solution, obtained by dissolving the biodegradable polymer and polyoxyethylene-derived block copolymer, be added, with stirring, to the polar phase.

Still further, Grandfils uses a surfactant (a cholesterol) to produce the nanoparticles. If the cholesterol surfactant were not added, microparticles, rather than nanoparticles, would have been formed.

Accordingly, Grandfils purposely avoids using a non-polar organic solvent when the polymer solution is mixed with the aqueous solution, and requires using a cholesterol surfactant when using the polar organic solvent. This is not the same as the invention as presently claimed in Claim 1, and dependent claims thereof. The Examiner is respectfully requested to withdraw the rejections.

With respect to Claims 12 and 13, directed to the nanoparticles produced by the method of Claims 1 and 2, since the process is patentable, the product produced by the product is also patentable.

Rejections under 35 U.S.C. 103 (a)

Claims 1-17 were rejected under 35 U.S.C. 103 (a) as obvious over Grandfils in view of U.S. Patent Application Publication No. 2004/0220081 to Kreitz et al. ("Kreitz"). The rejection is respectfully traversed if applied to the amended claims.

The claims

As stated above, the claims have been amended to specify that the method involves dissolving a biodegradable polymer, together with a polyoxyethylene-derived block copolymer, in a non-polar organic solvent. This is added, with stirring, to a polar phase, wherein the biodegradable polymer has low solubility. The polymer precipitates and forms the nanoparticles.

Grandfils

Grandfils does not use a non-polar organic solvent in the step of adding the polymer solution to the aqueous solvent.

Kreitz

Kreitz is directed to a method for preparing nanoparticles of a therapeutic, prophylactic or diagnostic agent. Kreitz's method involves dissolving the agent in a solvent to form a first solution, and providing a non-solvent for the agent, where the non-solvent is miscible with the solvent. The first solution is mixed with the non-solvent to form nanoparticles of the therapeutic, prophylactic or diagnostic agent.

Analysis

Kreitz teaches (Paragraph 0075) that "[t]he key requirements for selecting the non-solvent are that the agent is not soluble in the non-solvent, and that the non-solvent is sufficiently miscible with the solvent to form a single solvent phase after mixing."

Grandfils also teaches using a water-miscible solvent to dissolve the polymer and an aqueous phase in which to add the polymer solution.

In contrast, the claims as amended require using a non-polar organic solvent, which is added to a polar solvent, such as an aqueous solvent.

With respect to Grandfils, the present invention represents a significant improvement, in that a much simpler process is employed. The solution of polymers in the non-polar organic solvent can be directly mixed with the polar phase, generating nanoparticles with the desired properties, without an intermediate step of isolating a dried polymer blend either by solution and evaporation or by fusion.

Accordingly, the problem to be solved can be seen as the provision of a method for making nanoparticles which comprise a biodegradable polymer and a polyoxyethylene-derived block copolymer, which needs less intermediate steps than the processes disclosed in the cited references, and is therefore more efficient than such processes.

Indeed, Grandfils teaches away from the invention as now claimed, in that Grandfils teaches that where polymers based on biocompatible polyesters are previously dissolved in water-immiscible chlorinated organic solvents, there are problems such as a lack of control of particle size and in the particle loading of protein drugs (Col. 1, lines 53-64). Thus, one of skill in the art, reading Grandfils, would not seek to mix a non-polar solvent solution of these polymers with a polar phase to obtain the desired nanoparticles, since Grandfils teaches that it would be difficult to control the size and properties of the resulting polymers.

Further, Kreitz teaches away from using polymer excipients, when he states:

> However in some situations, the presence of an encapsulating polymer may be unnecessary, or even inhibiting, in the delivery of a drug. For example, for the delivery of a highly hydrophobic or otherwise poorly soluble drug, in which the dissolution of the drug is rate-limiting in delivery, no coating is needed to delay drug delivery or protect the drug from the action of a delivery route in the body...

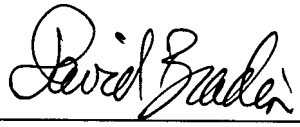
Paragraph 0013

For at least these reasons, the claims are non-obvious over the cited references.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,



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